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CORRELATION BETWEEN ISCHEMIC HEART DISEASE AND CHEMOTHERAPY

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ABSTRACT

Ischemic stroke is a condition diagnosed when a blood clot or malignant particle reduces or stops the blood flow to a part of the body. Chemotherapy is a treatment used to cure cancer by killing fast-growing cells redundant to its malignancy. Numerous cancer treatments have shown a statistical relationship with ischemic diseases. Through previous studies and statistics, this research paper will focus on the positive correlation between ischemic heart disease and chemotherapy. This is mainly due to the cause of venous thrombosis (VTE), a side effect generated by drugs used in neoadjuvant chemotherapy and chemotherapy. Substances such as colony-stimulating factors (CSF) and erythropoiesis-stimulating agents (ESA) are examples of substances that generate venous thrombosis. Venous thrombosis is a condition in which a patient's blood flow is impeded through blood clots in the blood vessel and leads to a thrombotic stroke, the most common form of an ischemic stroke. This subject shows significance in the field of medical science and medicine as it shows what factors of drugs used in chemotherapy influence the human blood vessels. Limitations exist in this paper as the lack of resources resulted in the paper being based on pure literature reviews from previous academic papers. Furthermore, specific sources that have been used in the paper were published a decade ago. This research aims to understand the extent of chemotherapy's influence on ischemic strokes and the factors of chemotherapy that cause ischemic strokes. This research paper was written using evidence derived from the experiments and conclusions of previous academic papers. It emphasizes the danger and addresses certain risks of chemotherapy, aiming to be a catalyst for the development of drugs that may combat ischemic strokes in the future.

KEYWORDS: Chemotherapy, Ischemic Strokes, Venous Thrombosis.

INTRODUCTION

Chemotherapy is a cancer treatment that focuses on killing fast growing cells redundant to its malignancy. Numerous studies have shown that drugs used during chemotherapy may cause venous thrombosis, which is the accumulation of clots in a blood vessel that could potentially lead to an ischemic heart disease (Rogers, 2003). Indeed, VTEs may act as plaques to cause thrombotic strokes, a leading cause of ischemic strokes (Raskob et al., 2014). Chemotherapeutic drugs such as methotrexate, 5-fluorouracil, cisplatin, tamoxifen, and L-asparaginase are all factors that may cause VTEs and strokes (Saynak et al., 2008; Esteva et al., 2006). These specific regimes are commonly used when preparing for conditions when proceeding with the chemotherapy process. For example, L-asparaginase is a drug commonly used for chemotherapy patients with breast cancer or childhood leukemia (Grisold et al., 2009). While this drug is used in induction therapies, the first phase of chemotherapy, it is also a drug well known for its association with forming VTEs (Rogers, 2003). Furthermore, neoadjuvant chemotherapy (NC) has been shown to increase the risk of short-term heart disease (Abt et al., 2014). According to Abt et al. (2014), a multivariable regression analysis stated that patients who undertook NCs had an increased risk of developing a stroke with neurological deficits.

In a study by Saini et al. (2021), an estimated 87% of all strokes were ischemic diseases. Inevitably, if a subject has a positive correlation with the number of strokes, this subject must be related to ischemic diseases. Specifically, studies have shown ADT, a drug used in chemotherapy, has increased the risk of stroke (Jespersen et al., 2014). This study shows that ADT patients have a highly increased risk of getting ischemic strokes.

A study by Kuan et al. (2014) analyzed statistics from a hospital in Taiwan. This analysis showed that chemotherapy was a factor that increased a patient's risk of developing ischemic strokes, along with age, hypertension, and diabetes. The study correlates chemotherapy and ischemic heart diseases by showing that the relative risk of ischemic diseases has gone up after a patient with ovarian cancer has taken chemotherapy. The study also mentions the detrimental side effects platinum compounds have on ischemic diseases (Kuan et al., 2014).

Furthermore, colony-stimulating factors and erythropoiesis-stimulating agents are used to prevent infections and neutropenia when a patient is taking chemotherapy. These drugs also relate to ischemic strokes, as they are considered a factor that also causes VTE. Additionally, two studies by Du and Zhang (2015; 2016) both showed that these colony-stimulating factors and erythropoiesis-stimulating agents have increased the risk of an ischemic heart stroke. Du and Zhang experimented by studying 80,925 patients taking chemotherapy with collateral cancer aged over 64 (2015). The results were definite, as they revealed that patients using CSFs and ESAs during their chemotherapy

were 58% more likely to develop VTE than patients who did not (Du et al., 2015).

In another study, Li et al. (2006) experimented by taking data from the Chang Gung Memorial Hospital from 1994 to 2004. These data show that a total of 10,963 patients were undertaking the chemotherapy process. In 1 month of chemotherapy, 15 patients experienced 16 ischemic heart strokes, leading to the deaths of 14 people (Li et al., 2006). This statistic shows that 0.137% of the patients experienced ischemic strokes after chemotherapy, while the normal rate of a person getting ischemic strokes is 0.035% (Li et al., 2006). This proves that the rate at which a person is diagnosed with an ischemic stroke may multiply after chemotherapy.

MATERIAL AND METHODS

The methods used in this research paper are literature reviews of academic papers relevant to this topic. A lot of experiments and research were conducted to find the relationship between chemotherapy and ischemic diseases. This paper uses previous experiments and organizes the results to state the correlation between chemotherapy and ischemic heart diseases. Both quantitative and qualitative research were done to find the results of the paper.

RESULTS

The results of the research paper conclude that chemotherapy does positively correlate with ischemic diseases. 11% of patients receiving chemotherapy had an incident of VTE. Moreover, specific chemotherapy drugs recorded a rate of up to a 20% risk of getting VTE when utilized (Haddad et al., 2006). Substances such as L-asparaginase are highly associated with producing VTEs, but their use is inevitable in some cases as the drug amplifies the effects of chemotherapy (Saynak et al., 2008). Furthermore, neoadjuvant drugs have also shown a role in increasing the risk of ischemia (Abt et al., 2014). For example, 5-fluorouracil is a neoadjuvant chemotherapy drug that increases the risk of heart disease and VTEs. Additionally, CSFs and ESAs are drugs that prevent infections and neutropenia that drastically contribute to causing ischemic heart diseases (Du et al., 2016). Another study states that platinum compounds, such as cisplatin, used in chemotherapy bear a higher risk of causing an ischemic disease (Kuan et al., 2014). The indicated drugs are all dangerous substances used in chemotherapy that may escalate the result of treating cancer but also increase the risk of ischemic diseases.

DISCUSSION

The purpose of this study was to understand the correlation between ischemic diseases and chemotherapy by identifying and examining the factors that relate to the two diseases. Previous studies have provided evidence regarding experimental studies relevant to statistics. An experiment conducted by Li et al. (2006) stated the increase in the risk of getting an ischemic disease. According to Roger (2003) and Du et al. (2015), a factor behind increasing the risk of ischemic strokes after chemotherapy is the drugs used in neoadjuvant chemotherapy for a greater ramification upon cancer (2003; 2016). Methotrexate, 5-fluorouracil, cisplatin, L-asparaginase, CSFs, and ESAs are all common drugs used to amplify the effects of chemotherapy. However, these substances have also proven to amplify the dangers of ischemia by generating venous thrombosis (Saynak et al., 2008; Esteva et al., 2006; Du et al., 2016).

Cancer is a major factor that increases one's risk of ischemia. Research by Chung et al. states that tumor patients face higher risks due to the release of microparticles into a patient's blood vessel. These microparticles may develop into VTEs, a main cause of ischemic diseases. According to Navi et al. (2018), 6.9% of elders diagnosed with lung cancer developed ischemic strokes, while only 3.2% of elders developed ischemic strokes without lung cancer. Another study shows that 10% of the patients with ischemic strokes also had comorbid cancer (Navi et al., 2018). These statistics state that some cancer patients potentially have double the risk of getting ischemic strokes compared to patients without cancer. Thus, cancer and ischemic strokes have a relative nature. While cancer is a factor that risks ischemic strokes before any treatment, chemotherapy has also been proven to increase the patient's risk of ischemia.

The significance of this study is exigent as chemotherapy is a widely known cancer treatment. Over one million people in the US alone are undergoing chemotherapy. Considering the risk of ischemic diseases cancer itself produces, chemotherapy must advance to minimize the risk of ischemia cancer patients' burden. The increase in the rate of ischemic disease caused by the side effects of chemotherapy must be examined carefully.

Limitations exist in this research paper as no experiments were conducted. This was due to a lack of resources, as no labs or hospitals granted permission for the study of chemotherapy's correlation to ischemic heart diseases. Due to this limitation, the paper was unable to advance its research question through relevant experiments and had to rely on previous studies and experiments. In addition, some sources from which this study drew information have aged around a decade. This limits the recency of the information and excludes information that may have been found in the current years.

Presumed Cause*	**Usual Cancer Type**	**Cancer-Related Risk Factors**
Cardioembolism		
Cardiomyopathy	Breast cancer	Anthracycline and Trastuzumab chemotherapy
Paradoxical embolism	Solid, hematologic, or primary brain tumors	Venous thromboembolism, immobility, and active chemotherapy
Other		
Cerebral vein thrombosis	Solid, hematologic, or primary brain tumors	L-asparaginase chemotherapy, tumors near venous sinuses

Table and Figures

Abbreviations: VEGF, vascular endothelial growth factor.

**Causes are listed in alphabetic order according to ASCO*

stroke subtype classification.

Note: Copyright by Navi et al. in 2018 "Ischemic Stroke in Cancer Patients: A Review of an Underappreciated Pathology". The following table shows that tumors from brains and breasts have been discovered by chemotherapy in Navi et al.'s (2018) research. This table clearly shows that the relationship between cancer and chemotherapy exists.

Table 2. Ischemic stroke mechanisms related to cisplatin-based chemotherapy
Hypomagnesemia-based vasospasm
Hyperreninemia or hyperaldosteronism
Platelet hyper aggregation
Monocyte procoagulant hyperactivity
Increased fibrinopeptide A
Decreased tissue activators
Endothelial dysfunction
Increased serum cholesterol levels

Table 2

Notes: Copyright by Saynak et al., 2008, "Chemotherapy and cerebrovascular disease"

The following table describes the negative impacts of cisplatin that lead to ischemic diseases. The table states the mechanisms cisplatin causes that increase a patient's risk of developing ischemic diseases.

CONCLUSION

The investigation elucidates a discernible correlation between chemotherapy and the incidence of ischemic heart disease, substantiated by the heightened risk of venous thromboembolism (VTE) associated with certain chemotherapeutic agents. As these medications are integral to cancer treatment, their role in exacerbating ischemic conditions necessitates critical attention. The conclusive evidence underscores the imperative for oncological therapies to evolve, minimizing ischemic complications without compromising efficacy.

Future research should pivot towards developing chemotherapeutic agents that retain anticancer potency while mitigating prothrombotic effects. Additionally, studies focusing on personalized medicine could identify patients at elevated risk, tailoring treatments to safeguard cardiovascular health

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